IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Wheeler	
Application No.: 09/875,805	
Filed: 6/5/2001	Group Art Unit: 1635
Title: Method for Preventing Aggregation of a Lipid:Nucleic Acid Complex	Examiner: Epps, J.L.
Attorney Docket No.: INEX.P-010	Confirmation No.: 5995

BRIEF FOR APPELLANT

This brief is filed in support of Applicants' Appeal from the final rejection mailed 3/21/2003. Consideration of the application and reversal of the rejections are respectfully urged.

Real Party in Interest

The real party in interest is Inex Pharmaceuticals Corporation.

Related Appeals and Interferences

To Applicants' knowledge there are no related appeals or interferences.

Status of Claims

Claims 1-14 are pending in this application. No other claims have been presented.

Status of Amendments

All amendments have been entered, and are reflected in the Appendix listing the claims on appeal.

Summary of Invention

Lipid:nucleic acid complexes are structures that can be used to introduce nucleic acids into cells for therapeutic purposes. One of the problems associated with such complexes, however, is a formation of aggregates of individual complexes, which are larger in size. US Patent No. 5,820,873 which is the reference relied on by the Examiner at issue herein discloses the desirablity of reducing aggregation and teaches a method for accomplishing this result through the incorporation of PEG-ceramide lipids in positively-charged lipid particles prior to complexation of the lipid particles with nucleic acids. The present invention provides an alternative approach to achieving the same result.

In accordance with a first aspect of the invention (claims 1-7), particle aggregation of lipid:nucleic acid complex particles is achieved by a method comprising the step of incorporating a non-cationic, polyethylene glycol (PEG)-modified lipid into a composition comprising lipid:nucleic acid complex particles. The lipid:nucleic acid complex particles are present before addition of the non-cationic lipid and comprise a cationic lipid and a nucleic acid polymer. In accordance with a second aspect of the invention (claims 8-14) a method is provided for preparing a lipid:nucleic acid complex. This method comprises the steps of:

(a) combining a nucleic acid with a cationic lipid to produce a lipid:nucleic acid complex; and

(b) mixing the lipid:nucleic acid complex with a non-cationic lipid which is a polyethylene glycol-based polymer, wherein the polyethylene glycol-based lipid reduces the tendency of the lipid:nucleic acid complex to aggregate.

Issue on Appeal

Are claims 1-14 anticipated by US Patent No. 5,820,873 of Choi et al, and therefore unpatentable under 35 USC § 102(b).

Grouping of Claims

All claims are argued as a single group and stand or fall together.

Argument

Claims 1-14 stand rejected under 35 USC § 102(b) as anticipated by Choi et al. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Independent claim 1 recites that the claimed method comprises the step of "incorporating a non-cationic lipid into a composition comprising lipid:nucleic acid complex particles," wherein the particles comprise a cationic lipid and a nucleic acid polymer, and wherein the non-cationic lipid is a polyethylene glycol-based polymer. The other independent claim, claim 8, recites step (a) which is forming a lipid:nucleic acid complex, and step (b) which is mixing this complex with a non-cationic lipid. Thus, these claims recite specific steps, performed in a specific order, and in order to anticipate the claim the Choi reference must teach the performance of these steps in this order. The Examiner has not shown this to be the case.

The Choi reference discloses lipid particles in which PEG-modified ceramide lipids are combined with other lipids into lipid particles. These PEG-ceramide particles are said, at Col. 4, lines 28-33, to be effective to prevent aggregation of liposomes incorporating DNA. This, however, does not amount to a teaching of the claimed method. One skilled in the art can readily imagine multiple possibilities for making PEG-ceramide-containing liposomes that incorporate DNA. The most obvious of these is making a PEG-Ceramide-containing liposome, and then adding DNA to the liposome. This order of steps flows from the disclosure of incorporating PEG-lipids into liposomes (Col. 13, llines 32-42; Examples 7 and 8) and the use of liposomes as

drug carriers (Cols. 14-18). This order of steps is different from that required by the present claims, which require that the PEG-Ceramide be added to a preestablished DNA:Lipid complex. Nothing in Choi teaches such an order of method steps, and thus Choi cannot be said to anticipate any of the present claims and the rejection should be reversed.

In the Official Action, the Examiner states that "contrary to Applicant's assertions, as stated in the prior Office Action, the PEG-modified ceramide lipids of Choi et al can be used in preventing aggregation of liposomes incorporating ... DNA." Applicants believe that the Examiner has failed to appreciate the argument being made. Applicants are not contesting that Choi teaches that if you make a liposome with PEG-ceramide in it, and then add DNA, that aggregation will be reduced. However, nothing in Choi teaches, or even suggests, that adding a PEG-modified ceramide to a pre-existing lipid:nucleic acid complex would result in any change in the aggregation behavior or in any other specific property of that complex.

In the Advisory Action, the Examiner states that the teaching in Choi of liposomes incorporating a targeting moiety, including DNA, "is interpreted as encompassing (sic, a method?) wherein the PEG-ceramide is used to prevent the aggregation of liposomes presently containing (i.e., 'incorporating') DNA. Therefore, Applicants arguments do not take the place of evidence that would suggest that the teachings of Choi et al. do not anticipate the claimed invention." To the extent this statement is understood, it appears that the Examiner may be trying to argue that Choi et al. discloses a genus that encompasses the claimed invention. This, however, is not sufficient to establish anticipation. *In re Arkley*, 172 U.S.P.Q. 524, 526-527 (CCPA 1972).

Alternatively, it may be that the Examiner is arguing that the claimed order of steps is inherent in Choi. Inherency can only be relied upon to support an anticipation rejection where the claimed invention (in this case including the order of the steps) is a necessary consequence of the explicit teaching. To establish anticipation under the theory of inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990). "Inherency . . . may not be established by

probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999).

The reference relied on this case teaches, in the only express teaching provided an order of steps as follows:

cationic lipid + non-cationic lipid ---> lipid particle

lipid particle + nucleic acid ---> lipid:nucleic acid complex

In contrast, the claimed invention specifies the following steps:

cationic lipid + nucleic acid ---> lipid:nucleic acid particle

lipid:nucleic acid particle + non-cationic lipid--->modified lipid:nucleic acid particle

These processes are different and accordingly there is no anticipation.

The rejection of claims 1-14 should be reversed.

Respectfully submitted,

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